

interest on a target protein to form a target protein-ligand conjugate, comprising detecting the formation of said target protein-ligand conjugate and identifying the ligand present in said conjugate by subjecting said conjugate directly, without prior fragmentation and without liberation of said ligand from said conjugate, to mass spectrometry analysis.

41. The method of claim 40 wherein said target protein is selected from the group consisting of an enzyme, a hormone, a transcription factor, a receptor, a ligand for a receptor, a growth factor and an immunoglobulin.

42. The method of claim 41 wherein said target protein is a cytokine receptor.

43. The method of claim 42 wherein said cytokine receptor is an interleukin receptor.

44. The method of claim 42 wherein said cytokine receptor is selected from the group consisting of receptors for erythropoietin (EPO), granulocyte colony stimulating factor, granulocyte macrophage colony stimulating factor, thrombopoietin (TPO), IL-2, IL-3, IL-4, IL-5, IL-6, IL-10, IL-11, and IL-12.

45. The method of claim 41 wherein said ligand is a cytokine.

46. The method of claim 45 wherein said cytokine is an interleukin.

47. The method of claim 41 wherein said cytokine is selected from the group consisting of erythropoietin (EPO), granulocyte colony stimulating factor, granulocyte macrophage colony stimulating factor, thrombopoietin (TPO), IL-2, IL-3, IL-4, IL-5, IL-6, IL-10, IL-11, and IL-12.

48. The method of claim 40 wherein said target protein comprises said chemically reactive group without prior modification of said target protein.

49. The method of claim 40 wherein said target protein has been modified to comprise said chemically reactive group.

50. The method of claim 40 wherein said chemically reactive group is a primary or secondary amine group which forms a Schiff base adduct with an aldehyde or ketone group present on said ligand.

51. The method of claim 40 wherein said chemically reactive group is an aldehyde or a ketone group which forms a Schiff base adduct with a primary or secondary amine group present on said ligand.

52. The method of claim 50 or claim 51 wherein said adduct is treated with a reducing agent prior to said mass spectrometry analysis.

53. The method of claim 40 wherein said chemically reactive group is a thiol group, masked thiol group, or activated thiol group, which forms a disulfide group with a thiol functionality present on said ligand.

54. The method of claim 53 wherein said target protein contains or is modified to contain no more than two thiol groups.

55. The method of claim 53 wherein said target protein contains or is modified to contain no more than one thiol group.

56. A mass spectrometer comprising a target protein-ligand conjugate comprising a small, non-oligomeric, soluble, synthetic organic ligand less than 500 daltons in size, that binds covalently to a chemically reactive group at a site of interest on a target protein to form a target protein-ligand conjugate.

57. A small, non-oligomeric, soluble, synthetic organic ligand less than 500 daltons in size, that binds covalently to a chemically reactive group at a site of interest on a target protein to

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form a target protein-ligand conjugate, identified by detecting the formation of said target protein-ligand conjugate and identifying the ligand present in said conjugate by subjecting said conjugate directly, without prior fragmentation and without liberation of said ligand from said conjugate, to mass spectrometry analysis. - -

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